The Examiner has objected to the specification for containing a typographical error in Table III. In this Amendment, Table III has been replaced with a new Table III in which the typographical error has been corrected. It is requested that the objection be withdrawn.

Claims 46-54 remain rejected under 35 U.S.C. 112, first paragraph, for containing new matter. The Examiner has taken the position that the peptide sequences that appeared in the originally filed Claim 1 are not SEQ ID NOs: 19-39. Therefore, the Examiner has stated that the original claims cannot be relied upon for support for these sequences.

It is submitted that the Examiner's position is not well taken. It is again submitted that original Claim 1, element (c), incorporated the sequences of Figures 1 and 2 into the language of Claim 1. As the sequences disclosed in Figures 1 and 2 correspond with SEQ ID NOs: 19-39 (among other sequences), it is submitted that the Examiner's position that the specification does not support the claims is not well taken.

Applicant thanks the Examiner for the courtesy shown to its representative during the September telephonic interview. It is submitted that the following is an accurate representation of the subjects discussed during that Interview. During the Interview, the Examiner discussed the disclosure of SEQ ID NOs: 19-39 in the original specification and claims. Based upon her memory (as the file was not available to the Examiner), the Examiner stated that the disclosures in the original specification and claims were insufficient because the sequences disclosed in the original claims were limited to fragments of the sequences. The Examiner also took the position that examples of the claimed invention were not disclosed in the specification.

It is submitted that the Examiner has confused this rejection with the rejection discussed in the following paragraphs and it is requested that the rejection be withdrawn for the above reasons and those that follow.

As can be seen from the Examiner's comments, it is submitted that the Examiner has taken the position that the specification does not teach the presently claimed invention. In particular, the Examiner has taken the position that the specification and original claims do not teach amino acid sequences with lengths of at least 6, 8, and 10 amino acids selected from SEQ ID NO:19-39. However, it is submitted that many of the sequences contained in originally filed Figure 2 do possess sequences longer than 10 amino acids in length. Therefore, the rejection is improper as the original disclosure teaches sequences longer than 10 amino acids in length.

Additionally, element (c) of original Claim 1 refers explicitly to the sequences of Figures 1 and 2 (i.e., the sequences of the pending Claims). Therefore, it is submitted that this rejection is improper in light of element (c) of the original Claim 1. It is requested that the rejection be withdrawn.

Claims 46-54 remain rejected under 35 U.S.C. 112, first paragraph, for lack of written description. The Examiner has taken the position that the specification discloses SEQ ID NOs: 2, 3, and 19-39, but that there is no disclosure of peptides or peptide derivatives of at least 6 amino acids and no more than 25 amino acids (i.e., the claimed invention). In other words, the rejection is based upon the apparent failure of the specification to list any examples of the claimed invention.

The Examiner has rejected Applicant's previous argument regarding MPEP section 2164.02 and the presence of working examples. The Examiner has taken the

position that the absence of working examples was not the issue, but that the written description of the invention is so broad that one of ordinary skill could not perform it based upon the description. As stated previously, the Examiner has taken the position that the specification and original claims do not disclose sequences of the length that are claimed in the present invention.

It is submitted that this rejection is not well taken because all of the sequences from SEQ ID NOs. 10-39 (which correspond to the sequences of the original application) fulfill the claimed length features (that is, a length of 6-25 amino acids). Additionally, it is submitted that in the experimental examples of the invention (see, for example, Examples 1.4, 4, and 5), concrete examples of peptides that fall within the scope of the present claims are disclosed. Therefore, it is submitted that the enablement rejection is improper in light of the explicit teachings contained in the present specification and it is requested that the rejection be withdrawn.

The Examiner has also objected to the incorporation of the Hammer reference into the specification. Attached to the Response is a declaration in which it is stated that the material added to the specification in the amendment dated 12/31/01 consists of the same material incorporated by reference in the referencing application. No new matter has been added.

The Examiner has also refused to grant priority to the claims beyond that of the present filing date. The Examiner has taken the position that the scope of the claimed invention is not contained in the priority applications. Additionally, the Examiner has refused to provide priority because a translation of the original priority applications have not been provided to her.

It is submitted that the priority requirements for the present application have already been fulfilled. Certified copies of the priority documents were filed in U.S. Serial No. 08/374,468 (filed January 18, 1995). The receipt of these documents had been confirmed by the Examiner in charge of that application on October 16, 1996. When the present application was filed on June 30, 1999 as a continuation application of 08/374,468, it was noted that the certified copies of the priority documents had already been filed in the parent application, thereby eliminating the need to provide new copies to the Patent Office. Therefore, this element of the priority requirements has been satisfied. Applicant also filed verified translations of the priority applications with our Response of December 31, 2001, thereby fulfilling the second requirement. Therefore, it is submitted that the rejection is not well taken.

Applicant has attached to this Response a petition (with copies of (a) the verified translations of the documents, (b) the return postcard, and (c) the relevant pages of the December 31, 2001 Response that refer to the priority documents attached thereto). It is requested that priority be granted in light of the proper submission of the priority documents on December 31, 2001.

Claims 46-53 remain rejected under 35 U.S.C. 102(b) as anticipated by WO 95/07992 (the "'992 application"). The Examiner has taken the position that the '992 application teaches a sequence that comprises at least six residues of the SEQ ID NO:19 sequence. The Examiner has advanced that the amendments to the claims were insufficient and that the presently drafted Claims 46 and 48 still read upon the '996 application. In particular, the Examiner has alleged that the claims still read upon a

peptide derivative which is not SEQ ID NO:19, but rather is amino acid residues 1-10 of SEQ ID NO:19.

However, it is submitted that the Examiner may have overlooked that section (a) of the claims were amended to recite "a peptide of at least 6 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 3, and 20-39." SEQ ID NO:19 is no longer part of the claims. Therefore, in light of this previous amendment, it is submitted that the rejection is not well taken and it is requested that the rejection be withdrawn.

Claims 52-54 remain rejected as obvious under 35 U.S.C. 103(a) in light of the '992 application and U.S. Patent Nos. 5,750,114 (the "'114 patent") and 6,060,309 (the "'309 patent"). The Examiner has taken the position that the amendments made to the claims were insufficient to overcome the combination of references. In particular, the Examiner has noted that the '992 application teaches a peptide derivative that is not SEQ ID NO:19, but contains the first 10 amino acid residues of SEQ ID NO: 19.

It is submitted that the citation of the '309 patent is improper as the '309 patent was filed after the priority date of the present application, thereby rendering the rejection not well taken (see above). Therefore, it is requested that the rejection be withdrawn.

The Examiner has issued a new ground of rejection against Claims 46-54. Claims 46-54 have been rejected under 35 U.S.C. 112, first paragraph, as not enabled. The Examiner has taken the position that the specification does not provide enablement for the making and/or using an isolated peptide/derivative and pharmaceutical of the type claimed in Claims 46-54. The Examiner has argued that the specification does not enable the claimed peptides of between 6 and 25 amino acids in length that possess at

least 6 amino acids from one of SEQ ID NO: 2, 3, or 19-39, and peptides of between 6 and 25 amino acid residues in length which are comprised of undisclosed amino acid residues other than anchor residues for binding to any allele of HLA-DR3 or HLA-DR4, or any peptide which exhibits a specificity and/or affinity that is equivalent to that of the afore mentioned peptides. The Examiner has also alleged that the state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed invention can be made and/or used.

In particular, the Examiner has alleged that the specification fails to provide any peptides or peptide derivatives that satisfy the requirements of Claims 52-54. Additionally, the Examiner has advanced that the specification fails to define critical terms, such as "a specificity or/and affinity." The Examiner has also stated that an undue amount of experimentation would be required to determine derivatives or peptides that are shorter than those described in the 1995 Immunogenetics Rammensee reference. The Examiner has based this contention on two grounds. First, she argues that numerous 6-25 residue combinations are possible. Further, she argues that it is uncertain whether all of the combinations would be capable of binding to HLA-DR3 or HLA-DR4. Second, the Examiner has argued that minimum amount of peptide required to span the binding groove and to make favorable contacts may be dependent upon the sequence of the peptide since different amino acid residues have different binding properties.

The Examiner has also argued that the Ngo reference teaches that the relationship between the sequence and its tertiary structure is not well understood and that it is not predictable. Therefore, the Examiner alleges that there would be a high

level of unpredictability in the claimed designing and selection of sequences. She also advances that the present specification fails to provide adequate guidance for developing the sequences that maintain the required function. Finally, the Examiner indicated that she has rebutted our previous arguments with the above contentions.

It is noted that the enablement rejection is based on a number of the same issues already raised in the previously discussed rejections. Therefore, Applicant relies on the previous comments for the overlapping bases of rejections. As for the lack of definitions (such as for "a specificity or/and affinity"), it is submitted that this term is well known in the art and that one of ordinary skill would recognize its meaning and what it is being claimed by its use.

Additionally, it is noted that the present specification discloses peptides which bind to particular MHC alleles. These peptides are suitable for screening peptide derivatives with the same or improved binding characteristics. This type of test is routine and is based upon the competition principle (that the binding of the comparative peptide to the MHC molecule is inhibited by the test peptide). Usually, a peptide according to the invention is labeled and presented as a "reporter peptide" and is bound to the corresponding MHC complex. Peptide analogs which show the same or improved binding capability to MHC molecules displace the reporter peptide. This displacement allows an easy determination of suitable analogs.

It is submitted that detailed instructions for producing peptide mimetica can be found in the specification on page 10, last paragraph. Additionally, the Hammer publication (1993) shows that phage libraries can also be used for identifying peptides

with equivalent binding characteristics without any problems. It is therefore requested that the rejection be withdrawn for this reason as well.

It is further submitted that the Examiner has misunderstood the Ngo reference. Ngo is concerned with the question of predicting protein structure from known polypeptide sequences. Therefore, only complex proteins are discussed, not short peptides. Therefore, it is submitted that Ngo is directed towards a completely different area of study and that it is not relevant to the present invention.

Additionally, it is submitted that the peptides of the present invention bind to a binding groove of MHC-complexes. It is not known whether these short peptides show any tertiary structure at all. However, it is known that no tertiary structure is required for binding to the MHC-binding groove. The peptides are present in this binding groove in a folded or more or less linear form and this would be known to any person of ordinary skill. Therefore, the present invention differs from the cited references in this manner as well. It is requested that the rejection be withdrawn for this and the previously listed reasons.

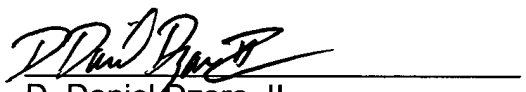
Finally, Claims 46-54 have been newly rejected under 35 U.S.C. 112, first paragraph, as not enabled by the specification. In particular, the Examiner has taken the position that the specification does not provide sufficient support for the making and using of an isolated peptide/derivative and pharmaceutical composition. It is submitted that the amendments made above to Claims 46-48 render this objection moot. The Claims have been limited to those MHC alleles specifically mentioned on page 11 of the specification. Therefore, it is requested that the rejection be withdrawn in light of the amendments to the claims.

Applicant respectfully urges that, in light of the above amendments and discussion, the claimed invention is in condition for allowance and request early notification to that effect.

In the event this paper is not timely filed, Applicant hereby petitions for an appropriate extension of time. The fee for this extension may be charged to our Deposit Account No. 01-2300, along with any other fees which may be due with respect to this paper.

Please charge any fee deficiency or credit any overpayment to Deposit Account No. 01-2300, referring to client-matter number 100564-09014.

Respectfully submitted,



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Enclosures: Marked-Up Copy of Specification
Marked-Up Copy of the Claims
Petition for Extension of Time (Two Months)
Copies of Documents (the verified translations of the documents, the return postcard, and the relevant pages of the December 31, 2001 Response that refer to the priority documents attached thereto)
Declaration

MARKED-UP COPY OF SPECIFICATION

TABLE III

Relative Position									
	1	2	3	4	5	6	7	8	9
[ORB1*0101] DRB1*0101	Y* (47%) F (26%)	X	X	M (48%) L (28%)	X	A (34%) G (23%) S (09%)	X	X	L (43%) M (13%) A (13%)
DRB1*0401	W (43%) Y (31%)	X	X	M (23%) A (19%) V (13%) L (12%)	X	T (60%) S (12%)	L (34%) Q (20%) M (10%) N (10%)	X	X
DRB1*1101	W (67%)	X	X	M (33%) L (23%) V (13%)	X	R (61%) K (12%)	X	X	X

MARKED-UP COPY OF THE CLAIMS

46. (Twice Amended) A peptide derived from glutamic acid decarboxylase having a length of at most 25 amino acids and comprising

(a) a peptide of at least 6 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NOS: 2, 3 and 20-39, or

(b) a peptide or peptide derivative having a length of 6 to 25 amino acids which exhibits a specificity or/and affinity which is equivalent to that of the peptide (a) and includes anchor positions for binding to alleles of MHC class II molecules DR3 or DR4, wherein the peptide derivative is not SEQ ID NO: 19, and wherein the alleles of MHC class II are selected from the group consisting of DR B1 101, DR B1 401, DR B1 402, DR B1 404, and DR B1 1601.

47. (Once Amended) The peptide of claim 46, wherein the peptide (a) includes anchor positions for binding to alleles of MHC class II molecules DR3 or DR4, and wherein the alleles of MHC class II are selected from the group consisting of DR B1 101, DR B1 401, DR B1 402, DR B1 404, and DR B1 1601.

48. (Twice Amended) The peptide of claim 46, wherein the peptide comprises

(a) a peptide of at least 6 amino acids of an amino acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO: 3, or

(b) a peptide or peptide derivative having a length of 6 to 25 amino acids which exhibits a specificity or/and affinity which is equivalent to that of the peptide (a) and includes anchor positions for binding to alleles of MHC class II molecules DR3 or DR4,

wherein the peptide derivative is not SEQ ID NO: 19, and wherein the alleles of MHC class II are selected from the group consisting of DR B1 101, DR B1 401, DR B1 402, DR B1 404, and DR B1 1601.